BCKDHA gene

branched chain keto acid dehydrogenase E1, alpha polypeptide

Normal Function

The *BCKDHA* gene provides instructions for making one part, the alpha subunit, of an enzyme complex (a group of enzymes that work together). This complex is called branched-chain alpha-keto acid dehydrogenase, or BCKD. Two alpha subunits connect with two beta subunits, which are produced from the *BCKDHB* gene, to form a critical part of the enzyme complex called the E1 component.

The BCKD enzyme complex is responsible for one step in the normal breakdown of three protein building blocks (amino acids). These amino acids—leucine, isoleucine, and valine—are obtained from the diet. They are present in many kinds of food, particularly protein-rich foods such as milk, meat, and eggs. The BCKD enzyme complex is active in mitochondria, which are specialized structures inside cells that serve as energy-producing centers. The breakdown of leucine, isoleucine, and valine produces molecules that can be used for energy.

Health Conditions Related to Genetic Changes

maple syrup urine disease

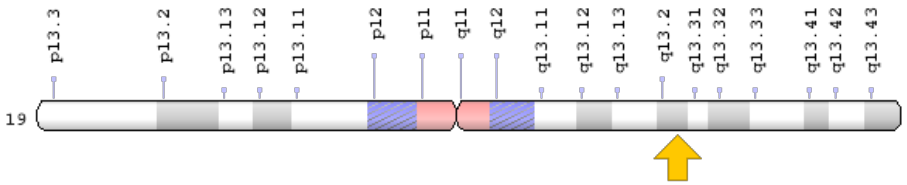
More than 40 mutations in the *BCKDHA* gene have been identified in people with maple syrup urine disease, most often in individuals with the severe, classic form of the disorder. Most *BCKDHA* mutations change single amino acids in the alpha subunit of the BCKD enzyme complex. In the Old Order Mennonite population, where maple syrup urine disease occurs frequently, the most common mutation replaces the amino acid tyrosine with the amino acid asparagine at position 438 (written as Tyr438Asn or Y438N).

Mutations in the *BCKDHA* gene disrupt the normal function of the BCKD enzyme complex, preventing it from effectively breaking down leucine, isoleucine, and valine. As a result, these amino acids and their byproducts build up in the body. This accumulation is toxic to cells and tissues, particularly in the nervous system. The buildup of these substances can lead to seizures, developmental delay, and the other medical problems associated with maple syrup urine disease.

Chromosomal Location

Cytogenetic Location: 19q13.2, which is the long (q) arm of chromosome 19 at position 13.2

Molecular Location: base pairs 41,397,789 to 41,425,005 on chromosome 19 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- BCKDE1A
- BCKDH E1-alpha
- branched chain keto acid dehydrogenase E1, alpha polypeptide (maple syrup urine disease)
- MSUD1
- ODBA_HUMAN

Additional Information & Resources

Educational Resources

- Basic Neurochemistry (sixth edition, 1998): Major pathways of branched-chain amino acid metabolism (figure) https://www.ncbi.nlm.nih.gov/books/NBK20436/figure/A3097/
- Basic Neurochemistry (sixth edition, 1998): Maple syrup urine disease was the first congenital defect of branched-chain amino acid catabolism to be described https://www.ncbi.nlm.nih.gov/books/NBK28225/#A3107

GeneReviews

- Maple Syrup Urine Disease https://www.ncbi.nlm.nih.gov/books/NBK1319

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28BCKDHA%5BTIAB%5D%29+OR+%28branched+chain+keto+acid+dehydrogenase+AND+E1+AND+alpha%5BTIAB%5D%29%29+OR+%28BCKD+AND+E1%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- BRANCHED-CHAIN KETO ACID DEHYDROGENASE E1, ALPHA POLYPEPTIDE
  http://omim.org/entry/608348

Research Resources

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=BCKDHA%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=986
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/593
- UniProt
  http://www.uniprot.org/uniprot/P12694

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